

<110> Yan, Rigiang Tomasselli, Alfredo G. Gurney, Mark E. Emmons, Thomas L. Bienkowski, Mike J. Heinrikson, Robert L. <120> SUBSTRATES AND ASSAYS FOR BETA-SECRETASE ACTIVITY <130> 29915/00281A.US <140> 09/908,943 <141> 2001-07-19 <150> 60/219.795 <151> 2000-07-19 <160> 199 <170> PatentIn Ver. 2.0 <210> 1 <211> 2070 <212> DNA <213> Homo sapiens <400> 1 atggcccaag ccctgccctg gctcctgctg tggatggcg cgggagtgct gcctgcccac 60 ggcacceage aeggcateeg getgeeeetg egeageggee tggggggege eeeeetgggg 120 gtggagatgg tggacaacct gaggggcaag tcggggcagg gctactacgt ggagatgacc 240 gtgggcagcc ccccgcagac gctcaacatc ctggtggata caggcagcag taactttgca 300 gtgggtgctg cccccaccc cttcctgcat cgctactacc agaggcagct gtccagcaca 360 taccgggacc tccggaaggg tgtgtatgtg ccctacaccc agggcaagtg ggaaggggag 420 ctgggcaccg acctggtaag catcccccat ggccccaacg tcactgtgcg tgccaacatt 480 getgecatea etgaateaga eaagttette ateaaegget eeaaetggga aggeateetg 540 gggctggcct atgctgagat tgccaggcct gacgactccc tggagccttt ctttgactct 600 ctggtaaagc agacccacgt teccaacete ttetecetge acetttgtgg tgetggette 660 ceceteaace agtetgaagt getggeetet gteggaggga geatgateat tggaggtate 720 gaccactcgc tgtacacagg cagtctctgg tatacaccca tccggcggga gtggtattat 780 gaggtcatca ttgtgcgggt ggagatcaat ggacaggatc tgaaaatgga ctgcaaggag 840 tacaactatg acaagagcat tgtggacagt ggcaccacca accttcqttt gcccaaqaaa 900 gtgtttgaag ctgcagtcaa atccatcaag gcagceteet ccaeggagaa gtteeetgat 960 ggtttctggc taggagagca gctggtgtgc tggcaagcag gcaccacccc ttggaacatt 1020 ttcccagtca tctcactcta cctaatgggt gaggttacca accagtcctt ccgcatcacc 1080 atcetteege ageaatacet geggeeagtg gaagatgtgg ceaegteeca agacgaetgt 1140 tacaagtttg ceateteaca gteateeacg ggeaetgtta tgggagetgt tateatggag 1200 ggcttctacg ttgtctttga tcgggcccga aaacgaattg gctttgctgt cagcgcttgc 1260 catgtgcacg atgagttcag gacggcagcg gtggaaggcc cttttgtcac cttggacatg 1320

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<212> PRT

<213> Homo sapiens

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Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser 20 25 30

Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
35 40 45 .

Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
50 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser 85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val 115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp 130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile 145 150 155 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp 165 170 175

Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp 180 185 190

Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro 195 200 205

Asn Leu Phe Ser Leu His Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln 210 215 220

Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Gly Gly Ile 225 230 235 240

Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg 245 250 255

Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln 260 265 270

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val 275 280 285 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala 295 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp 315 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg 360 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala 375 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu 420 · 425 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala 455 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp 470 475 Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile Ser Leu Leu Lys 500 <210> 3 <211> 1977 <212> DNA <213> Homo sapiens atggcccaag ccctgccctg gctcctgctg tggatgggcg cgggagtgct gcctgcccac 60 ggcacccage acggcatccg gctgcccctg cgcagcggcc tggggggcgc ccccctgggg 120 gtggagatgg tggacaacct gaggggcaag tcggggcagg gctactacgt ggagatgacc 240 gtgggcagcc ccccgcagac gctcaacatc ctggtggata caggcagcag taactttgca 300 gtgggtgctg cccccaccc cttcctgcat cgctactacc agaggcagct gtccagcaca 360 taccgggacc tccggaaggg tgtgtatgtg ccctacaccc agggcaagtg ggaaggggag 420 ctgggcaccg acctggtaag catcccccat ggccccaacg tcactgtgcg tgccaacatt 480 gctgccatca ctgaatcaga caagttette atcaaegget ccaaetggga aggeateetg 540 gggctggcct atgctgagat tgccaggctt tgtggtgctg gcttccccct caaccagtct 600 gaagtgctgg cctctgtcgg agggagcatg atcattggag gtatcgacca ctcgctgtac 660 acaggcagtc tctggtatac acccatccgg cgggagtggt attatgaggt gatcattgtg 720 cgggtggaga tcaatggaca ggatctgaaa atggactgca aggagtacaa ctatgacaag 780 agcattgtgg acagtggcac caccaacett cgtttgccca agaaagtgtt tgaagctgca 840

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Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
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                             40
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
                 85
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
                                105
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
                        135
Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
                    150
                                        155
Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
                                    170
Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Leu Cys Gly
Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly
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Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu 210 215 220

Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val 225 230 235 240

Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr 245 250 255

Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu 260 265 270

Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser 275 280 285

Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val 290 295 300

Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser 305 310 315 320

Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile 325 330 335

Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln 340 345 350

Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val
355
360
365

Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala 370 375 380

Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu 385 390 395 400

Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu 405 410 415

Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr 420 425 430

Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu 435 440 445

Cys Leu Met Val Cys Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln 450 455 460

His Asp Asp Phe Ala Asp Asp Ile Ser Leu Leu Lys 465 470 475

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<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: synthetic
 peptide sequence

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<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence: synthetic
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Lys Val Glu Ala Asn Tyr Glu Val Glu Gly Glu Arg Cys Lys
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<210> 7
<211> 14
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Lys Val Glu Ala Asn Tyr Ala Val Glu Gly Glu Arg Lys Lys
<210> 8
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<213> Artificial Sequence
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Glu Ala Asn Tyr Glu Val Glu Phe
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<211> 8
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<400> 10
Gly Val Leu Leu Ala Ala Gly Trp
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<210> 11
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Ile Ile Lys Met Asp Asn Phe Gly
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Asp Ser Ser Asn Leu Glu Met Thr His Ala
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<222> (7)
<223> Xaa=cysteic acid
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Thr His Gly Phe Gln Leu Xaa His
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<211> 8
<212> PRT
<213> Artificial Sequence
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Cys Tyr Thr His Ser Phe Ser Pro
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<221> SITE
<222> (7)
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<210> 16
<211> 8
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<223> Xaa= any amino acid
<220>
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<222> (4)..(7)
<223> Xaa= any amino acid
<400> 16
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<222> (4)..(7)
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<211> 10
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                                     10
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<211> 10
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                5
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<211> 10
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Lys
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Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val
Phe Phe Ala Glu
<210> 26
<211> 16
<212> PRT
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Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
<210> 27
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<223> Xaa= cysteic acid
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Leu Val Xaa Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Ala

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<222> (7)
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<223> Xaa=cysteic acid
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<221> SITE
<222> (20)
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                                     10
Glu Asn Tyr Xaa Asn
<210> 29
<211> 23
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Tyr Arg Tyr Gln Ser His Asp Tyr Ala Phe Ser Ser Val Glu Lys Leu
Leu His Ala Leu Gly Gly Cys
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<210> 30
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Leu His Ala Leu Gly Gly Cys
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Arg Gly Ser Met Ala Gly Val Leu
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<400> 34

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<210> 39
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<212> PRT
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<210> 40
<211> 5
<212> PRT
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<400> 40
Val Gly Ser Gly Val
<210> 41
<211> 12
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence: synthetic
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<222> (9)
<223> Xaa= cysteic acid
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<210> 42
<211> 15
<212> PRT
<213> Artificial Sequence
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Trp Arg Arg Val Glu Ala Leu Tyr Leu Val Glu Gly Glu Arg Lys
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<210> 43
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<400> 43
Lys Val Glu Ala Asn Tyr Leu Val Glu Gly Glu Arg Lys
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                                     10
<210> 44
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Met Leu Leu Leu
 1
<210> 45
<211> 6
<212> PRT
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     peptide sequence
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Asp Ala Ala His Pro Gly
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<211> 14
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<400> 46
Lys Val Glu Ala Asn Tyr Asp Val Glu Gly Glu Arg Lys Lys
                  5
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<211> 14
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<400> 47
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                  5
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<210> 48
<211> 14
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Lys Val Glu Ala Leu Tyr Ala Val Glu Gly Glu Arg Lys Lys
                 5
                                      10
<210> 49
<211> 8
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<223> Description of Artificial Sequence: synthetic
     peptide sequence
<220>
<221> SITE
<222> (1)
<223> Xaa = E, G, I, D, T, cysteic acid or S
<400> 49
Xaa Ala Asn Tyr Glu Val Glu Phe
<210> 50
<211> 8
<212> PRT
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<223> Description of Artificial Sequence: synthetic
      peptide sequence
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<222> (2)
<223> Xaa= A, V, I, S, H, Y, T or F
Glu Xaa Asn Tyr Glu Val Glu Phe
 1
                  5
<210> 51
<211> 8
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<220>
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<221> SITE
<222> (3)
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<400> 51
Glu Ala Xaa Tyr Glu Val Glu Phe
  1
<210> 52
<211> 8
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<220>
<221> SITE
<222> (4)
<223> Xaa= Y, L, M, Nle, F or H
<400> 52
Glu Ala Asn Xaa Glu Val Glu Phe
 1
                  5
<210> 53
<211> 8
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<220>
<221> SITE
<222> (5)
<223> Xaa= E, A, D, M, Q, S or G
<400> 53
Glu Ala Asn Tyr Xaa Val Glu Phe
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<210> 54
<211> 8
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<220>
<221> SITE
<222> (6)
<223> Xaa= V, A, N, T, L, F or S.
<400> 54
Glu Ala Asn Tyr Glu Xaa Glu Phe
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peptide sequence

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Xaa Phe Ala Xaa Xaa Xaa Xaa
                5
<210> 113
<211> 9
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 113
Glu Val Asn Leu Asp Ala Glu Phe Arg
                  5
<210> 114
<211> 7
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 114
Asp Tyr Lys Asp Asp Asp Lys
                  5
<210> 115
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 115
Ala Cys Gly Ser Glu Ser Met Asp Ser Gly Ile Ser Leu Asp Asn Lys
                  5
                                     10
Trp
<210> 116
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 116
Trp Lys Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Lys
                  5
                                                         15
```

```
Lys .
```

```
<210> 117
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 117
Ala Asn Leu Ser Thr Phe Ala Gln Pro Arg Arg
<210> 118
<211> 22
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 118
Tyr Arg Tyr Gln Ser His Asp Tyr Ala Phe Ser Ser Val Glu Lys Leu
                  5
Leu His Leu Gly Gly Cys
             20
<210> 119
<211> 22
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 119
Tyr Arg Tyr Gln Ser His Asp Tyr Ala Phe Ser Ser Val Glu Lys Leu
Leu His Leu Gly Gly Cys
             20
<210> 120
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 120
Lys Thr Ile Thr Leu Glu Val Glu Pro Ser
```

1

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<210> 121
<211> 12
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<220>
<221> SITE
<222> (9)
<223> Xaa= cysteic acid
<400> 121
Val Glu Ala Leu Tyr Leu Val Cys Xaa Gly Glu Arg
                  5
<210> 122
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 122
Val Glu Ala Leu Tyr Leu Val Glu Gly Glu Arg
 1
                  5
<210> 123
<211> 363
<212> PRT
<213> Homo sapiens
<220>
<223> galactosyltransferase
<400> 123
Met Ala Ser Lys Ser Trp Leu Asn Phe Leu Thr Phe Leu Cys Gly Ser
                                     10
Ala Ile Gly Phe Leu Leu Cys Ser Gln Leu Phe Ser Ile Leu Leu Gly
                                 25
Glu Lys Val Asp Thr Gln Pro Asn Val Leu His Asn Asp Pro His Ala
Arg His Ser Asp Asp Asn Gly Gln Asn His Leu Glu Gly Gln Met Asn
                         55
Phe Asn Ala Asp Ser Ser Gln His Lys Asp Glu Asn Thr Asp Ile Ala
```

Glu Asn Leu Tyr Gln Lys Val Arg Ile Leu Cys Trp Val Met Thr Gly

Pro Gln Asn Leu Glu Lys Lys Ala Lys His Val Lys Ala Thr Trp Ala 105 Gln Arg Cys Asn Lys Val Leu Phe Met Ser Ser Glu Glu Asn Lys Asp Phe Pro Ala Val Gly Leu Lys Thr Lys Glu Gly Arg Asp Gln Leu Tyr Trp Lys Thr Ile Lys Ala Phe Gln Tyr Val His Glu His Tyr Leu Glu Asp Ala Asp Trp Phe Leu Lys Ala Asp Asp Asp Thr Tyr Val Ile Leu 170 Asp Asn Leu Arg Trp Leu Leu Ser Lys Tyr Asp Pro Glu Glu Pro Ile Tyr Phe Gly Arg Arg Phe Lys Pro Tyr Val Lys Gln Gly Tyr Met Ser Gly Gly Ala Gly Tyr Val Leu Ser Lys Glu Ala Leu Lys Arg Phe Val 215 Asp Ala Phe Lys Thr Asp Lys Cys Thr His Ser Ser Ser Ile Glu Asp 225 230 235 Leu Ala Leu Gly Arg Cys Met Glu Ile Met Asn Val Glu Ala Gly Asp Ser Arg Asp Thr Ile Gly Lys Glu Thr Phe His Pro Phe Val Pro Glu 265 His His Leu Ile Lys Gly Tyr Leu Pro Arg Thr Phe Trp Tyr Trp Asn 280 Tyr Asn Tyr Tyr Pro Pro Val Glu Gly Pro Gly Cys Cys Ser Asp Leu Ala Val Ser Phe His Tyr Val Asp Ser Thr Thr Met Tyr Glu Leu Glu 310 315 Tyr Leu Val Tyr His Leu Arg Pro Tyr Gly Tyr Leu Tyr Arg Tyr Gln Pro Thr Leu Pro Glu Arg Ile Leu Lys Glu Ile Ser Gln Ala Asn Lys Asn Glu Asp Thr Lys Val Lys Leu Gly Asn Pro 355

<210> 124

<211> 405

<212> PRT

<213> Homo sapiens

<220>

<223> Homo sapiens sialylytransferase 1

<400> 124

Ile His Thr Asn Leu Lys Lys Lys Phe Ser Cys Cys Val Leu Val Phe

Leu Leu Phe Ala Val Ile Cys Val Trp Lys Glu Lys Lys Lys Gly Ser Tyr Tyr Asp Ser Phe Lys Leu Gln Thr Lys Glu Phe Gln Val Leu Lys Ser Leu Gly Lys Leu Ala Met Gly Ser Asp Ser Gln Ser Val Ser Ser Ser Ser Thr Gln Asp Pro His Arg Gly Arg Gln Thr Leu Gly Ser Leu . 75 Arg Gly Leu Ala Lys Ala Lys Pro Glu Ala Ser Phe Gln Val Trp Asn Lys Asp Ser Ser Ser Lys Asn Leu Ile Pro Arg Leu Gln Lys Ile Trp 105 Lys Asn Tyr Leu Ser Met Asn Lys Tyr Lys Val Ser Tyr Lys Gly Pro Gly Pro Gly Ile Lys Phe Ser Ala Glu Ala Leu Arg Cys His Leu Arg 135 Asp His Val Asn Val Ser Met Val Glu Val Thr Asp Phe Pro Phe Asn Thr Ser Glu Trp Glu Gly Tyr Leu Pro Lys Glu Ser Ile Arg Thr Lys 170 Ala Gly Pro Trp Gly Arg Cys Ala Val Val Ser Ser Ala Gly Ser Leu 185 Lys Ser Ser Gln Leu Gly Arg Glu Ile Asp Asp His Asp Ala Val Leu Arg Phe Asn Gly Ala Pro Thr Ala Asn Phe Gln Gln Asp Val Gly Thr 215 Lys Thr Thr Ile Arg Leu Met Asn Ser Gln Leu Val Thr Thr Glu Lys 225 230 235 Arg Phe Leu Lys Asp Ser Leu Tyr Asn Glu Gly Ile Leu Ile Val Trp 250 Asp Pro Ser Val Tyr His Ser Asp Ile Pro Lys Trp Tyr Gln Asn Pro 265 Asp Tyr Asn Phe Phe Asn Asn Tyr Lys Thr Tyr Arg Lys Leu His Pro Asn Gln Pro Phe Tyr Ile Leu Lys Pro Gln Met Pro Trp Glu Leu Trp 295 Asp Ile Leu Gln Glu Ile Ser Pro Glu Glu Ile Gln Pro Asn Pro Pro 305 310 315 Ser Ser Gly Met Leu Gly Ile Ile Ile Met Met Thr Leu Cys Asp Gln

Val Asp Ile Tyr Glu Phe Leu Pro Ser Lys Arg Lys Thr Asp Val Cys

Tyr Tyr Gln Lys Phe Phe Asp Ser Ala Cys Thr Met Gly Ala Tyr 355 360 365

His Pro Leu Leu Tyr Glu Lys Asn Leu Val Lys His Leu Asn Gln Gly 370 375 380

Thr Asp Glu Asp Ile Tyr Leu Leu Gly Lys Ala Thr Leu Pro Gly Phe 385 390 395 400

Arg Thr Ile His Cys 405

<210> 125

<211> 518

<212> PRT

<213> Homo sapiens

<220>

<223> Homo sapiens aspartyl protease 1

<400> 125

Met Gly Ala Leu Ala Arg Ala Leu Leu Leu Pro Leu Leu Ala: Gln Trp

1 5 10 15

Leu Leu Arg Ala Ala Pro Glu Leu Ala Pro Ala Pro Phe Thr Leu Pro 20 25 30

Leu Arg Val Ala Ala Ala Thr Asn Arg Val Val Ala Pro Thr Pro Gly 35 40 45

Pro Gly Thr Pro Ala Glu Arg His Ala Asp Gly Leu Ala Leu 50 55 60

Glu Pro Ala Leu Ala Ser Pro Ala Gly Ala Ala Asn Phe Leu Ala Met 65 70 75 80

Val Asp Asn Leu Gln Gly Asp Ser Gly Arg Gly Tyr Tyr Leu Glu Met 85 90 95

Leu Ile Gly Thr Pro Pro Gln Lys Leu Gln Ile Leu Val Asp Thr Gly
100 105 110

Ser Ser Asn Phe Ala Val Ala Gly Thr Pro His Ser Tyr Ile Asp Thr 115 120 125

Tyr Phe Asp Thr Glu Arg Ser Ser Thr Tyr Arg Ser Lys Gly Phe Asp 130 135 140

Val Thr Val Lys Tyr Thr Gln Gly Ser Trp Thr Gly Phe Val Gly Glu 145 150 155 160

Asp Leu Val Thr Ile Pro Lys Gly Phe Asn Thr Ser Phe Leu Val Asn 165 170 175

Ile Ala Thr Ile Phe Glu Ser Glu Asn Phe Phe Leu Pro Gly Ile Lys 180 185 190

Trp Asn Gly Ile Leu Gly Leu Ala Tyr Ala Thr Leu Ala Lys Pro Ser 195 200 205

Ser Ser Leu Glu Thr Phe Phe Asp Ser Leu Val Thr Gln Ala Asn Ile 215 Pro Asn Val Phe Ser Met Gln Met Cys Gly Ala Gly Leu Pro Val Ala Gly Ser Gly Thr Asn Gly Gly Ser Leu Val Leu Gly Gly Ile Glu Pro Ser Leu Tyr Lys Gly Asp Ile Trp Tyr Thr Pro Ile Lys Glu Glu Trp Tyr Tyr Gln Ile Glu Ile Leu Lys Leu Glu Ile Gly Gly Gln Ser Leu 280 Asn Leu Asp Cys Arg Glu Tyr Asn Ala Asp Lys Ala Ile Val Asp Ser Gly Thr Thr Leu Leu Arg Leu Pro Gln Lys Val Phe Asp Ala Val Val Glu Ala Val Ala Arg Ala Ser Leu Ile Pro Glu Phe Ser Asp Gly Phe Trp Thr Gly Ser Gln Leu Ala Cys Trp Thr Asn Ser Glu Thr Pro Trp 345 Ser Tyr Phe Pro Lys Ile Ser Ile Tyr Leu Arg Asp Glu Asn Ser Ser 360 Arg Ser Phe Arg Ile Thr Ile Leu Pro Gln Leu Tyr Ile Gln Pro Met Met Gly Ala Gly Leu Asn Tyr Glu Cys Tyr Arg Phe Gly Ile: Ser Pro 390 395 Ser Thr Asn Ala Leu Val Ile Gly Ala Thr Val Met Glu Gly Phe Tyr Val Ile Phe Asp Arg Ala Gln Lys Arg Val Gly Phe Ala Ala Ser Pro Cys Ala Glu Ile Ala Gly Ala Ala Val Ser Glu Ile Ser Gly Pro Phe Ser Thr Glu Asp Val Ala Ser Asn Cys Val Pro Ala Gln Ser Leu Ser Glu Pro Ile Leu Trp Ile Val Ser Tyr Ala Leu Met Ser Val Cys Gly 470 475 Ala Ile Leu Leu Val Leu Ile Val Leu Leu Leu Pro Phe Arg Cys Gln Arg Arg Pro Arg Asp Pro Glu Val Val Asn Asp Glu Ser Ser Leu 500 . 505

<210> 126

Val Arg His Arg Trp Lys 515 <211> 255

<212> PRT

<213> Homo sapiens

<220>

<223> Homo sapiens syntaxin 6

<400> 126

Met Ser Met Glu Asp Pro Phe Phe Val Val Lys Gly Glu Val Gln Lys

1 10 15

Ala Val Asn Thr Ala Gln Gly Leu Phe Gln Arg Trp Thr Glu Leu Leu
20 25 30

Gln Asp Pro Ser Thr Ala Thr Arg Glu Glu Ile Asp Trp Thr Thr Asn
35 40 45

Glu Leu Arg Asn Asn Leu Arg Ser Ile Glu Trp Asp Leu Glu Asp Leu
50 60

Asp Glu Thr Ile Ser Ile Val Glu Ala Asn Pro Arg Lys Phe Asn Leu 65 70 75 80

Asp Ala Thr Glu Leu Ser Ile Arg Lys Ala Phe Ile Thr Ser Thr Arg 85 90 95

Gln Val Val Arg Asp Met Lys Asp Gln Met Ser Thr Ser Ser Val Gln $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110 \hspace{1.5cm}$

Ala Leu Ala Glu Arg Lys Asn Arg Gln Ala Leu Leu Gly Asp Ser Gly 115 120 125

Ser Gln Asn Trp Ser Thr Gly Thr Thr Asp Lys Tyr Gly Arg Leu Asp 130 135 140

Arg Glu Leu Gln Arg Ala Asn Ser His Phe Ile Glu Glu Gln Gln Ala 145 150 155 160

Gln Gln Gln Leu Ile Val Glu Gln Gln Asp Glu Gln Leu Glu Leu Val 165 170 175

Ser Gly Ser Ile Gly Val Leu Lys Asn Met Ser Gln Arg Ile Gly Gly 180 185 190

Glu Leu Glu Glu Gln Ala Val Met Leu Glu Asp Phe Ser His Glu Leu 195 200 205

Glu Ser Thr Gln Ser Arg Leu Asp Asn Val Met Lys Lys Leu Ala Lys 210 220

Val Ser His Met Thr Ser Asp Arg Gln Trp Cys Ala Ile Ala Ile 225 230 235 240

Leu Phe Ala Val Leu Leu Val Val Leu Ile Leu Phe Leu Val Leu 245 250 255

<210> 127

<211> 1728

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: nucleic acid encoding recombinant fusion protein

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<400> 127
atgetgetge tgetgetget getgggeetg aggetaeage tetecetggg cateateeea 60
gttgaggagg agaaccegga cttctggaac egegaggeag eegaggeeet gggtgeegee 120
aagaagctgc agcctgcaca gacagccgcc aagaacctca tcatcttcct gggcgatggg 180
atgggggtgt ctacggtgac agctgccagg atcctaaaag ggcagaagaa ggacaaactg 240
gggcctgaga tacccctggc catggaccgc ttcccatatg tggctctgtc caagacatac 300
aatgtagaca aacatgtgcc agacagtgga gccacagcca cggcctacct gtgcggggtc 360
aagggcaact tecagaceat tggettgagt geageegeee getttaacea gtgeaacaeg 420
acacgoggca acgaggtcat ctccgtgatg aatcgggcca agaaagcagg gaagtcagtg 480
ggagtggtaa ccaccacag agtgcagcac gcctcgccag ccggcaccta cgcccacacg 540
gtgaaccgca actggtactc ggacgccgac gtgcctgcct cggcccgcca ggagggtgc 600
caggacateg ctacgcaget catetecaac atggacattg acgtgateet aggtggagge 660
cgaaagtaca tgtttcccat gggaacccca gaccctgagt acccagatga ctacagccaa 720
ggtgggacca ggctggacgg gaagaatctg gtgcaggaat ggctggcgaa gcgccagggt 780 gcccggtatg tgtggaaccg cactgagctc atgcaggctt ccctggaccc gtctgtgacc 840
catctcatgg gtctctttga gcctggagac atgaaatacg agatccaccg agactccaca 900
ctggacccct ccctgatgga gatgacagag gctgccctgc gcctgctgag caggaacccc 960
egeggettet teetettegt ggagggtggt egeategace atggteatea tgaaageagg 1020
gettaceggg caetgaetga gaegateatg ttegaegaeg ceattgagag ggegggeeag 1080-
ctcaccagcg aggaggacac gctgagcctc gtcactgccg accactccca cgtcttctcc 1140
tteggagget acceetgeg agggagetee atetteggge tggceeetgg caaggeeegg 1200
gacaggaagg cctacacggt cctcctatac ggaaacggtc caggctatgt gctcaaggac 1260
ggcgcccggc cggatgttac cgagagcgag agcgggagcc ccgagtatcg gcagcagtca 1320
geagtgeece tggaegaaga gaeceaegea ggegaggaeg tggeggtgtt egegegge 1380
ccgcaggcgc acctggttca cggcgtgcag gagcagacct tcatagcgca cgtcatggcc 1440
ttegeegeet geetggagee etaeaeegee tgegaeetgg egeeeeege eggeaeeaee 1500
gacgccgcgc acccaggtaa ctatgaagtt gaattccgaa gagcactcta cgtagagggt 1560
gaaagaggat tettetacae teeaaaggea etetaceteg tagagggtga aagaggatte 1620
ttctacacta gtctcatgac catagcctat gtcatggctg ccatctgcgc cctcttcatg 1680
ctgccactct gcctcatggt ggactacaag gatgatgatg acaagtag
<210> 128
<211> 575
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: recombinant
      fusion protein sequence
Met Leu Leu Leu Leu Leu Leu Gly Leu Arg Leu Gln Leu Ser Leu
Gly Ile Ile Pro Val Glu Glu Asn Pro Asp Phe Trp Asn Arg Glu
Ala Ala Glu Ala Leu Gly Ala Ala Lys Lys Leu Gln Pro Ala Gln Thr
Ala Ala Lys Asn Leu Ile Ile Phe Leu Gly Asp Gly Met Gly Val Ser
Thr Val Thr Ala Ala Arg Ile Leu Lys Gly Gln Lys Lys Asp Lys Leu
Gly Pro Glu Ile Pro Leu Ala Met Asp Arg Phe Pro Tyr Val Ala Leu
Ser Lys Thr Tyr Asn Val Asp Lys His Val Pro Asp Ser Gly Ala Thr
```

Ala	Thr	Ala 115	Tyr	Leu	Cys	Gly	Val 120	Lys	Gly	Asn	Phe	Gln 125	Thr	Ile	Gly
				Ala							Thr	Thr	Arg	Gly	Asn

110

100

Glu Val Ile Ser Val Met Asn Arg Ala Lys Lys Ala Gly Lys Ser Val 145 150 155 160

Gly Val Val Thr Thr Arg Val Gln His Ala Ser Pro Ala Gly Thr 165 170 175

Tyr Ala His Thr Val Asn Arg Asn Trp Tyr Ser Asp Ala Asp Val Pro 180 185 190

Ala Ser Ala Arg Gln Glu Gly Cys Gln Asp Ile Ala Thr Gln Leu Ile 195 200 205

Ser Asn Met Asp Ile Asp Val Ile Leu Gly Gly Gly Arg Lys Tyr Met 210 225 220

Phe Pro Met Gly Thr Pro Asp Pro Glu Tyr Pro Asp Asp Tyr Ser Gln 225 235 240

Gly Gly Thr Arg Leu Asp Gly Lys Asn Leu Val Gln Glu Trp Leu Ala 245 250 255

Lys Arg Gln Gly Ala Arg Tyr Val Trp Asn Arg Thr Glu Leu Met Gln 260 265 270

Ala Ser Leu Asp Pro Ser Val Thr His Leu Met Gly Leu Phe Glu Pro 275 280 285

Gly Asp Met Lys Tyr Glu Ile His Arg Asp Ser Thr Leu Asp Pro Ser 290 295 300

Leu Met Glu Met Thr Glu Ala Ala Leu Arg Leu Leu Ser Arg Asn Pro 305 310 315 320

Arg Gly Phe Phe Leu Phe Val Glu Gly Gly Arg Ile Asp His Gly His 325 330 335

His Glu Ser Arg Ala Tyr Arg Ala Leu Thr Glu Thr Ile Met Phe Asp 340 345 350

Asp Ala Ile Glu Arg Ala Gly Gln Leu Thr Ser Glu Glu Asp Thr Leu 355 360 365

Ser Leu Val Thr Ala Asp His Ser His Val Phe Ser Phe Gly Gly Tyr 370 375 380

Pro Leu Arg Gly Ser Ser Ile Phe Gly Leu Ala Pro Gly Lys Ala Arg 385 390 395 400

Asp Arg Lys Ala Tyr Thr Val Leu Leu Tyr Gly Asn Gly Pro Gly Tyr
405
410
415

Val Leu Lys Asp Gly Ala Arg Pro Asp Val Thr Glu Ser Glu Ser Gly 420 425 430

Ser Pro Glu Tyr Arg Gln Gln Ser Ala Val Pro Leu Asp Glu Glu Thr 440 His Ala Gly Glu Asp Val Ala Val Phe Ala Arg Gly Pro Gln Ala His 455 Leu Val His Gly Val Gln Glu Gln Thr Phe Ile Ala His Val Met Ala Phe Ala Ala Cys Leu Glu Pro Tyr Thr Ala Cys Asp Leu Ala Pro Pro 485 Ala Gly Thr Thr Asp Ala Ala His Pro Gly Asn Tyr Glu Val Glu Pro 505 Arg Arg Ala Leu Tyr Val Glu Gly Glu Arg Gly Phe Phe Tyr Thr Pro 525 Lys Ala Leu Tyr Leu Val Glu Gly Glu Arg Gly Phe Phe Tyr Thr Ser 535 Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met 555 550 Leu Pro Leu Cys Leu Met Val Asp Tyr Lys Asp Asp Asp Lys 570 565 <210> 129 <211> 5 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: synthetic peptide sequence <400> 129 Lys Met Asp Ala Glu <210> 130 <211> 5 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: synthetic peptide sequence <400> 130 Gly Arg Arg Gly Ser <210> 131 <211> 10 <212> PRT <213> Artificial Sequence <220>

<223> Description of Artificial Sequence: synthetic

peptide sequence

```
<400> 131
  Val Glu Ala Asn Tyr Glu Val Glu Gly Glu
                    5
  <210> 132
  <211> 10
  <212> PRT
<213> Artificial Sequence
  <220>
  <223> Description of Artificial Sequence: synthetic
       peptide sequence
  <400> 132
  Val Glu Ala Asn Tyr Ala Val Glu Gly Glu
                    5
  <210> 133
 <211> 10
  <212> PRT
  <213> Artificial Sequence
  <220>
  <223> Description of Artificial Sequence: synthetic
       peptide sequence
  <400> 133
  Lys Thr Ile Asn Leu Glu Val Glu Pro Ser
                   5
  <210> 134
  <211> 10
  <212> PRT
  <213> Artificial Sequence
  <220>
  <223> Description of Artificial Sequence: synthetic
        peptide sequence
  <220>
  <221> MOD_RES
  <222> (5)
  <223> Nle
  <400> 134
  Lys Thr Ile Asn Xaa Glu Val Glu Pro Ser
                    5
  <210> 135
  <211> 10
  <212> PRT
  <213> Artificial Sequence
  <220>
  <221> MOD_RES
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<222> (5)
<223> Nle
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 135
Lys Thr Ile Asn Xaa Glu Val Asp Pro Ser
                  5
                                     10
 1
<210> 136
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<221> MOD RES
<222> (5)
<223> Nle
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 136
Lys Thr Ile Asn Xaa Asp Val Asp Pro Ser
                  5
<210> 137
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 137
Lys Thr Ile Ser Leu Asp Val Glu Pro Ser
 1
                5
                                     1.0
                            1
<210> 138
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 138
Lys Thr Ile Ser Leu Asp Val Asp Pro Ser
 1
                  5
<210> 139
<211> 4
<212> PRT
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 139
Lys Met Asp Ala
  1
<210> 140
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 140
Ser Tyr Glu Val
 1
<210> 141
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 141
Ser Glu Val Ser Tyr Glu Val Glu Phe Arg
<210> 142
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 142
Asn Leu Asp Ala
 1
<210> 143
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 143
Ser Glu Val Ser Tyr Asp Ala Glu Phe Arg
```

```
<210> 144
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 144
Ser Glu Val Ser Tyr Glu Ala Glu Phe Arg
                  5.
 1
<210> 145
<211> 25
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 145
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
                                     10
Glu Val Ser Tyr Glu Val Glu Phe Arg
                               25
             20
<210> 146
<211> 20
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 146
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Ser Tyr Glu
                  5
Val Glu Phe Arg
             20
<210> 147
<211> 15
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 147
Lys Thr Glu Glu Ile Ser Glu Val Ser Tyr Glu Val Glu Phe Arg
                  5
                                     10
```

```
<210> 148
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 148
Thr Glu Val Ser Tyr Glu Val Glu Phe Arg
                  5
<210> 149
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 149
Ser Glu Val Asp Tyr Glu Val Glu Phe Arg
 1.
                  5
<210> 150
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 150
Thr Glu Val Asp Tyr Glu Val Glu Phe Arg
                  5
<210> 151
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence .
<400> 151
Thr Glu Ile Asp Tyr Glu Val Glu Phe Arg
                  5
<210> 152
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
```

peptide sequence

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<400> 152
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg
                  5
<210> 153
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 153
Ser Glu Ile Asp Tyr Glu Val Glu Phe Arg
<210> 154
<211> 13
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (11)
<223> Xaa=tryptophan
<223> Description of Artificial Sequence: synthetic
      peptide sequence
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
<210> 155
<211> 18
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (16)
<223> Xaa=tryptophan
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 155
Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa
 1
                  5
                                      10
Lys Lys
<210> 156
<211> 23
```

```
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE .
<222> (21)
<223> Xaa=tryptophan
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 156
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val
Glu Phe Arg Xaa Lys Lys
        20
<210> 157
<211> 28
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<220>
<221> SITE
<222> (26)
<223> Xaa=tryptophan
<400> 157
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
<210> 158
<211> 13
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (11)
<223> Xaa=tryptophan
<223> Description of Artificial Sequence: synthetic
     peptide sequence
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
                                     10
<210> 159
<211> 18
```

```
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<220>
<221> SITE
<222> (16)
<223> Xaa=tryptophan
<400> 159
Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg
Xaa Lys Lys
<210> 160
<211> 23
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (21)
<223> Xaa=tryptophan
<220>
<223> Description of Artificial Sequence: synthetic
     peptide
<400> 160
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr
                                      10
Glu Val Glu Phe Arg Xaa Lys Lys
<210> 161
<211> 28
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (26)
<223> Xaa=tryptophan
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 161
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile
                                      10
                                                          15
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
```

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<210> 162
<211> 13
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (11)
<223> Xaa=oregon green
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 162
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
<210> 163
<211> 18
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (16)
<223> Xaa=oregon green
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 163
Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa
                                     10
Lys Lys
<210> 164
<211> 23
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (21)
<223> Xaa=oregon green
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 164
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu
                                      10
                                                          15
Val Glu Phe Arg Xaa Lys Lys
```

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<210> 165
<211> 28
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (26)
<223> Xaa=oregon green ·
<223> Description of Artificial Sequence: synthetic peptide sequence
<400> 165
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
                                      10
Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
             20
<210> 166
<211> 13
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (11)
<223> Xaa=oregon green
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 166
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
<210> 167
<211> 18
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (16)
<223> Xaa=oregon green
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 167
Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg
                  5
                                      10
Xaa Lys Lys
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<210> 168
<211> 23
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (21)
<223> Xaa=oregon green
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 168
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr
Glu Val Glu Phe Arg Xaa Lys Lys
                20
<210> 169
<211> 28
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (26)
<223> Xaa=oregon green
<223> Description of Artificial Sequence: synthetic .
      peptide sequence
<400> 169
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
                20
<210> 170
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 170
Ser Glu Val Asn Tyr Glu Val Glu Phe Arg
                  5
<210> 171
<211> 47
<212> DNA
<213> Artificial Sequence
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<223>	Description of Artificial Sequence: synthetic primer for site-directed mutagenesis of APP	
<400> gagato	171 etctg aaattagtta tgaagtagaa tteegaeatg aeteagg	47
<210><211><211><212><213>	48	
<220> <223>	Description of Artificial Sequence: synthetic primer for site-directed mutagenesis of APP	
<400> tgagto	172 Catgt cggaatteta etteataaet aattteagag ateteete	48
<210><211><212><212><213>	47	
<220> <223>	Description of Artificial Sequence: synthetic primer for site-directed mutagenesis of APP	
<400> gagato		47
<210><211><212><212><213>	48	
<220> <223>	Description of Artificial Sequence: synthetic primer for site-directed mutagenesis of APP	
<400> tgagto	174 catgt cggaatteta etteataaet aettteagag ateteete	48
<210><211><212><212><213>	47	
<220> <223>	Description of Artificial Sequence: synthetic primer for site-directed mutagenesis of APP	
<400> gagato	175 ctctg aaattagtta tgaagcagaa ttccgacatg actcagg	47
<210><211><211><212><213>	48	
<220> <223>	Description of Artificial Sequence: synthetic primer for site-directed mutagenesis of APP	

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<400> 176
tgagtcatgt cggaattctg cttcataact aatttcagag atctcctc
<210> 177
<211> 5
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 177
Val Ser Tyr Glu Val
<210> 178
<211> 5
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 178
Val Ser Tyr Asp Ala
 1
<210> 179
<211> 5
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 179
Ile Ser Tyr Glu Val
                  5
 1
<210> 180
<211> 5
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 180
Val Lys Met Asp Ala
  1
                  5
<210> 181
<211> 47
<212> DNA
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence: synthetic
      primer for generating mutant construct named
      MBPC125-SYEV
<400> 181
                                                                   47
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<210> 182
<211> 48
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      primer for generating mutant construct named
      MBPC125-SYEV
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                                                                   48
<210> 183
<211> 6
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 183
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 1
                  5
<210> 184
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 184
Val Glu Ala Asn Tyr Glu Val Glu Gly Glu
                  5 .
<210> 185
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 185
Val Glu Ala Asn Tyr Ala Val Glu Gly Glu
                  5
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<210> 186
<211> 8
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 186
Asp Tyr Lys Asp Asp Asp Lys
                  5
<210> 187
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 187
Ser Tyr Glu Ala
 1
<210> 188
<211> 4
<212> PRT
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     peptide sequence
<400> 188
Ser Tyr Ala Val
<210> 189
<211> 5
<212> PRT
<213> Artificial Sequence
<220,>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 189
Val Ser Tyr Glu Ala
 1
<210> 190
<211> 13
<212> PRT
<213> Artificial sequence
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<220>
<223> Description of artificial sequence: synthetic peptide sequence
<400> 190
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Trp Lys Lys
<210> 191
<211> 23
<212> PRT
<213> Artificial sequence
<220>
<223> Description of artificial sequence: synthetic peptide sequence
<400> 191
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu
Val Glu Phe Arg Trp Lys Lys
<210> 192
<211> 15
<212> PRT
<213> Artificial sequence
<220>
<223> Description of artificial sequence: synthetic peptide sequence
<220>
<221> SITE
<222> (1)..(1)
<223> amino acid at position 1 is biotinylated
<220>
<221> SITE
<222> (14)..(14)
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<223> cys at position 14 is derivatized with an oregon green

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<400> 192
Lys Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Lys
<210> 193
<211> 22
<212> PRT
<213> Artificial sequence
<220>
<223> Description of artificial sequence: synthetic peptide sequence
<220>
<221> SITE
<222> (1)..(1)
<223> amino acid at position 1 is biotinylated
<220>
<221> SITE
<222> (21)..(21)
<223> cys at position 21 is derivatized with an oregon green
<400> 193
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu
Val Glu Phe Arg Lys Lys
<210> 194
<211> 6806
<212> DNA
<213> Artificial sequence
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<223> Description of artificial sequence: synthetic DNA sequence <400> 194 60 ccgacaccat cgaatggcgc aaaacctttc gcggtatggc atgatagcgc ccggaagaga gtcaattcag ggtggtgaat gtgaaaccag taacgttata cgatgtcgca gagtatgccg 120 gtgtctctta tcagaccgtt tcccgcgtgg tgaaccaggc cagccacgtt tctgcgaaaa 180 cgcgggaaaa agtggaagcg gcgatggcgg agctgaatta cattcccaac cgcgtggcac 240 aacaactggc gggcaaacag tegttgctga ttggcgttgc cacetccagt ctggccctgc 300 360 acgcgccgtc gcaaattgtc gcggcgatta aatctcgcgc cgatcaactg ggtgccagcg tggtggtgtc gatggtagaa cgaagcggcg tcgaagcctg taaagcggcg gtgcacaatc 420. ttctcgcgca acgcgtcagt gggctgatca ttaactatcc gctggatgac caggatgcca 480 ttgctgtgga agctgcctgc actaatgttc cggcgttatt tcttgatgtc tctgaccaga 540 cacccatcaa cagtattatt ttctcccatg aagacggtac gcgactgggc gtggagcatc 600 tggtcgcatt gggtcaccag caaatcgcgc tgttagcggg cccattaagt tctgtctcgg 660 cgcgtctgcg tctggctggc tggcataaat atctcactcg caatcaaatt cagccgatag 720 cggaacggga aggcgactgg agtgccatgt ccggttttca acaaaccatg caaatgctga 780 atgagggcat cgttcccact gcgatgctgg ttgccaacga tcagatggcg ctgggcgcaa 840 tgcgcgccat taccgagtcc gggctgcgcg ttggtgcgga tatctcggta gtgggatacg 900 acgataccga agacagctca tgttatatcc cgccgttaac caccatcaaa caggattttc 960 1020 gcctgctggg gcaaaccagc gtggaccgct tgctgcaact ctctcagggc caggcggtga agggcaatca gctgttgccc gtctcactgg tgaaaagaaa aaccaccctg gcgcccaata 1080 cgcaaaccgc ctctccccgc gcgttggccg attcattaat gcagctggca cgacaggttt 1140 cccgactgga aagcgggcag tgagcgcaac gcaattaatg tgagttagct cactcattag 1200 . gcacaattct catgtttgac agcttatcat cgactgcacg gtgcaccaat gcttctggcg 1260 teaggeagee ateggaaget gtggtatgge tgtgeaggte gtaaateaet geataatteg 1320 tgtcgctcaa ggcgcactcc cgttctggat aatgtttttt gcgccgacat cataacggtt 1380 ctggcaaata ttctgaaatg agctgttgac aattaatcat cggctcgtat aatgtgtgga 1440 attgtgageg gataacaatt teacacagga aacagecagt eegtttaggt gtttteacga 1500 gcacttcacc aacaaggacc atagattatg aaaactgaag aaggtaaact ggtaatctgg 1560 attaacggcg ataaaggcta taacggtctc gctgaagtcg gtaagaaatt cgagaaagat 1620 accggaatta aagtcaccgt tgagcatccg gataaactgg aagagaaatt cccacaggtt 1680 geggeaactg gegatggeee tgacattate ttetgggeae acgacegett tggtggetae 1740

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caacgcggcc tttttacggt tcctggcctt ttgctggcct tttgctcaca tgttctttcc
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                                                                     5880
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<210> 195
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<220>

<223> Description of artificial sequence: synthetic peptide sequence

<220>

<221> MOD RES

<222> (1)..(1)

<211> 13

<212> PRT

<213> Artificial sequence

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<223> ACETYLATION (MCA)
 <220>
<221> SITE
<222> (11)..(11)
 <223> 2,4-dinitrophenyl group after the Lys at position 11
<400> 195
 Ser Glu Val Asn Leu Asp Ala Glu Phe Arg Lys Arg Arg
 <210> 196
 <211> 12
 <212> PRT
 <213> Artificial sequence
 <220>
 <223> Description of artificial sequence: synthetic peptide sequence
 <220>
 <221> SITE
 <222> (4)..(4)
 <223> amino acid at position 4 has been derivatized with a statine
 <400> 196
 Ser Glu Val Asn Val Ala Glu Phe Arg Gly Gly Cys
 <210> 197
 <211> 10
 <212> PRT
 <213> synthetic peptide sequence
 <220>
 <221> SITE
 <222> (4)..(4)
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<223> amino acid at position 4 has been derivatized with a statine

<220>

<221> SITE

<222> (10)..(10)

<223> amino acid at position 10 has been derivatized with Bodipy FL

<400> 197

Ser Glu Val Asn Val Ala Glu Phe Arg Cys 1 5 10

<210> 198

<211> 2043

<212> DNA

<213> Mus musculus

<400> 198 60 atggeeceag egetgeactg geteetgeta tgggtggget egggaatget geetgeecag ggaacceate teggeateeg getgeeeett egeagegee tggeagggee acceetggge 120 ctgaggctgc cccgggagac tgacgaggaa tcggaggagc ctggccggag aggcagcttt 180 gtggagatgg tggacaacct gaggggaaag tccggccagg gctactatgt ggagatgacc 240 gtaggcagcc ccccacagac gctcaacatc ctggtggaca cgggcagtag taactttgca 300 gtgggggctg ccccacaccc tttcctgcat cgctactacc agaggcagct gtccagcaca 360 tatcgagacc tccgaaaggg tgtgtatgtg ccctacaccc agggcaagtg ggaggggaa 420 ctgggcaccg acctggtgag catccctcat ggccccaacg tcactgtgcg tgccaacatt 480 gctgccatca ctgaatcgga caagttcttc atcaatggtt ccaactggga gggcatccta 540 gggctggcct atgctgagat tgccaggccc gacgactctt tggagccctt ctttgactcc 600 ctggtgaagc agacccacat tcccaacatc ttttccctgc agctctgtgg cgctggcttc 660 cccctcaacc agaccgaggc actggcctcg gtgggaggga gcatgatcat tggtggtatc 720 gaccactege tatacaeggg cagtetetgg tacacaecea teeggeggga gtggtattat 780 gaagtgatca ttgtacgtgt ggaaatcaat ggtcaagatc tcaagatgga ctgcaaggag 840 tacaactacg acaagagcat tgtggacagt gggaccacca accttcgctt gcccaagaaa 900 gtatttgaag ctgccgtcaa gtccatcaag gcagcctcct cgacggagaa gttcccggat 960 ggcttttggc taggggagca gctggtgtgc tggcaagcag gcacgacccc ttggaacatt 1020 ttcccagtca tttcacttta cctcatgggt gaagtcacca atcagtcctt ccgcatcacc 1080 1140 atccttcctc agcaatacct acggccggtg gaggacgtgg ccacgtccca agacgactgt

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Gly Leu Ala Gly Pro Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp 35 40 45

Glu Glu Ser Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val 50 55 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser 85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val 115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile 155 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp 185 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Ile Pro 200 Asn Ile Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln 215 Thr Glu Ala Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln 260 265 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val 280 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp 310 315 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val 345 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala 375 Val Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu 390 395 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Ala Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala 450 455 460

Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp 465 470 475 480

Ile Ser Leu Leu Lys 500